

Solvent	Dilution (D) and Washing (W)	Yield(%)	N ₉ - N ₇ Isomers	Temp	NaOH
DMF	D: Toluene W: Toluene/Acetone		N ₉ -(79%); N ₇ -(18%)	160°C	+
DMF	D: Toluene W: Toluene/Acetone	83%	N ₉ -(77%); N ₇ -(19%)	150°C	+
DMF	D: Toluene W: Toluene/Acetone, crystallize	70%		160°C	+
DMF	D: Toluene W: Toluene/EtOH(cold)	67%		150°C	+
DMF	D: Toluene W: Toluene/Acetone, crystallize	56%		130°C	NaOEt
DMF	D: Toluene W: Toluene/EtOH(cold)		N ₉ -(55%); N ₇ -(12%) Un-reacted starting	160°C	-
DMF	D: Toluene W: Toluene/EtOH(cold)	70%	N ₉ -(83%); N ₇ -(6%)	150°C	-
DEF	D: Toluene W: Toluene/EtOH(cold)	89%	N ₉ -(77%); N ₇ -(21%)	150°C	+
DMA	D: Toluene W: Toluene/EtOH(cold)	70%	N ₉ -(85%); N ₇ -(6%)	150°C	+
DMA	D: Toluene W: Toluene/EtOH(cold)	84%	N ₉ -(73%); N ₇ -(19.5%)	150°C	-

Table 1

Figure 1

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Solvent	Dilution (D) and Washing (W)	Yield(%)	N ₉ - N ₇ Isomers	Temp	NaOH
DMA	D: None, evaporated to dryness and t-BME added W: t-BME		N ₉ -(76%); N ₇ -(20%)	150°C	+
DMA	D: None, evaporated to dryness and CH ₃ CN added W: CH ₃ CN		N ₉ -(80%); N ₇ -(16%)	150°C	+
DMA	D: None, evaporated to dryness and EtOH added W: EtOH	67%	N ₉ -(90%); N ₇ -(4%)	150°C	+
DMA	D: None, evaporated to dryness and IPA added W: IPA	84%	N ₉ -(99%); N ₇ -(2%)	150°C	+
DMA	D: None, evaporated to dryness and IPA/CH ₃ CN (1:1) added W: IPA/CH ₃ CN (1:1)		N ₉ -(95.25%); N ₇ -(2.49%)	150°C	+
DMA	D: Evaporated to half in volume and Toluene added W: Toluene/ EtOH(cold)	87%	N ₉ -(76%); N ₇ -(12%)	160°C	+
DMA	D: Evaporated to half in volume and Toluene added W: Toluene/ EtOH(cold)	89%	N ₉ -(68%); N ₇ -(15%)	140°C	+

Table 2

Figure 2

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Solvent	Dilution (D) and Washing (W)	Yield(%)	N ₆ - N ₇ Isomers	Temp	Cat
DMA	D: CH ₃ CN W: CH ₃ CN		N ₆ -(88%), N ₇ -(11%)	150°C	+
DMA	D: EtOAc W: EtOAc	89%	N ₆ -(90%), N ₇ -(8%)	150°C	+
DMA	D: Toluene W: Toluene/EtOH (cold)		N ₆ -(95%), N ₇ -(5%)	150°C	+
DMA	D: Toluene W: IPA (cold)		N ₆ -(86%), N ₇ -(13%)	150°C	+
DMA	D: IPA W: IPA (cold)			150°C	+
DMA	D: IPA W: IPA	87%		160°C	+
DMA	D: IPA W: IPA	82%		140°C	+
DMA	D: t-BME W: IPA	87%	N ₆ -(95%), N ₇ -(2-78%)	150°C	+
DMF	D: Toluene W: Toluene/EtOH (cold)		N ₆ -(91%), N ₇ -(3%)	Reflux	+

Table 3

Figure 3

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HPLC METHOD

Column	SYNERGI 5 μ , 150 x 4.6 mm Phenomenex (C18)							
Mobile Phase	A 20 mM KH_2PO_4 pH 6.2 Buffer (KOH) B Acetonitrile							
Flow Rate	1.00 mL/min							
Gradient Table	<table><tr><td>0-15 min</td><td>0-60% B</td></tr><tr><td>15-17 min</td><td>60-0% B</td></tr><tr><td>17-19 min</td><td>0% B</td></tr></table>		0-15 min	0-60% B	15-17 min	60-0% B	17-19 min	0% B
0-15 min	0-60% B							
15-17 min	60-0% B							
17-19 min	0% B							
Column Temperature	35 °C							
Sample Temperature	6 °C (Autosampler)							
Sample Concentration	0.5 mg /mL (Water)							
Injection Volume	10 μ L							
Detection Wavelength	220, 270 nm							

Figure 4

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WO 2004/014912

PCT/US2002/025540

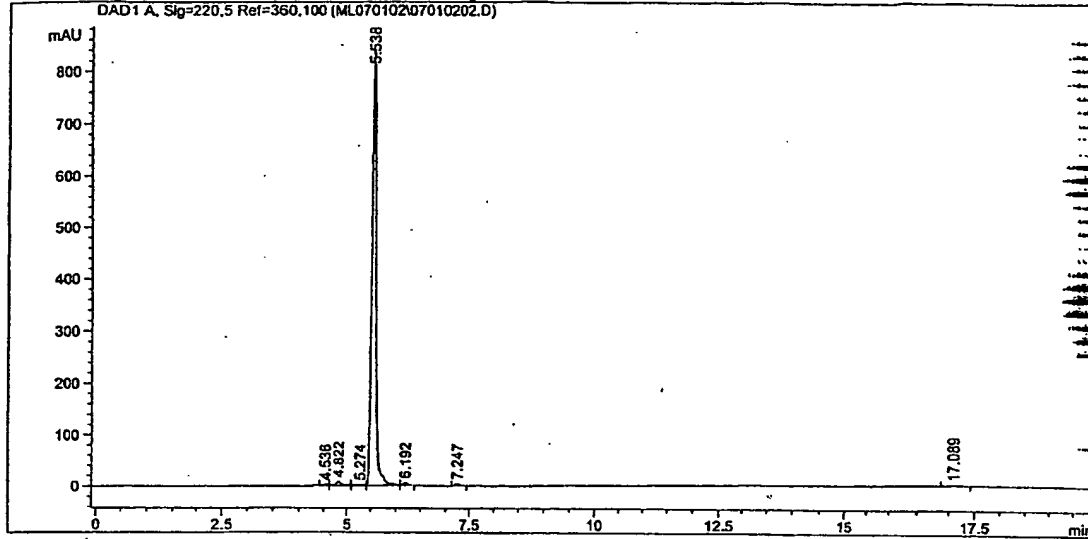
ata File C:\HPCHEM\1\DATA\ML070102\07010202.D

Sample Name: ICN373

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=====
Injection Date : 7/1/2002 5:16:33 PM      Seq. Line : 2
Sample Name    : ICN373-87                Location  : Vial 1
Acq. Operator  : Mike Landesman           Inj       : 1
                                           Inj Volume: 5 µl
Acq. Method    : C:\HPCHEM\1\METHODS\ICN34952.M
Last changed   : 6/14/2002 11:49:33 AM by Mike Landesman
Analysis Method: C:\HPCHEM\1\METHODS\ICN34929.M
Last changed   : 6/25/2002 8:19:23 AM by Mike Landesman
=====
DAD1 A, Sig=220,5 Ref=360,100 (ML070102\07010202.D)

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Area Percent Report
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Sorted By      : Signal
Multiplier     : 1.0000
Dilution      : 1.0000

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Signal 1: DAD1 A, Sig=220,5 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.536	VV	0.1116	22.60877	3.00970	0.4351
2	4.822	VV	0.1320	74.46996	8.04190	1.4331
3	5.274	VV	0.1676	18.32598	1.48883	0.3527
4	5.538	VV	0.0929	5003.10547	847.37561	96.2821
5	6.192	VB	0.1016	35.53940	5.34228	0.6839
6	7.247	PB	0.0963	24.99750	4.03450	0.4811
7	17.089	BB	0.2136	17.25084	1.21556	0.3320

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Totals :                5196.29793  870.50839
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Figure 5

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